CHAPTER II.1: INTRODUCTION TO THE COSTS OF CANCERS

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CHAPTER II.1: INTRODUCTION TO THE COSTS OF CANCERS

This section of the handbook contains chapters that describe costs of medical treatments for a variety of cancers that have been associated with exposure to environmental agents. Cancer is one of the three leading causes of death in the United States and throughout the world (Williams and Weisburger, 1993). It is a serious illness that has been associated with environmental exposures in both human and animal studies. Cancers often have similar treatment options (e.g., radiation, chemotherapy, surgery, reconstructive and physical therapy treatments), and generally require long-term medical care. Most occur with much greater frequency in individuals in the second half of life.

This section contains an overview of the environmental causes of cancer and general issues related to economic valuation of the medical treatment of cancer. It also contains an estimate of the cost of a "typical" cancer case and examples of how the typical cost estimates can be modified to obtain more information on specific cancers (using liver and bone cancers as examples). This chapter is followed by chapters containing medical cost information on specific types of cancer that may be associated with exposure to environmental agents.

II.1.A. Description

Cancer is the common term for all malignant tumors and includes carcinomas and sarcomas, depending on the tissue of origin. Cancer is characterized by abnormal growth that preys on the host. It may metasticize to other locations in the body and often leads to debilitation and/or death if left untreated. A critical distinction among tumors is made between benign and malignant tumors. Although benign tumors may be medically important and sometimes become malignant (Robbins et al., 1984), they are not considered cancerous, and so are not included in the cost estimates presented in this section.

II.1.B. Concurrent Effects

Concurrent effects commonly occur with cancer. These effects usually arise from two main causes: 1) as a result of a metastatic (spreading) process, leading to cancers at more than one site in the body, 2) as a result of the impaired health status of the cancer patient. Impaired health can arise from either the cancer's interference with normal functioning, or the adverse effects associated with chemotherapy, radiation treatment, surgery, or other medical treatments. Many of the side effects of cancer treatment are well known. For example, the antineoplastic drug adriamycin causes damage to the heart muscle. Radiation therapy may cause toxicity (e.g., sterility) and additional cancers while limiting the spread of cancer at the

original site. A variety of other effects are associated with cancer therapies. One focus in oncology is on balancing the toxic properties of the anticancer therapies in the health portions of the body against the need to cause toxicity to the tumor cells.

Because there are no benign cancer therapies, and cancer is often a metastatic process, there are invariably some costs associated with cancer that are not considered when only the direct medical costs of treating the primary cancer are considered. Some researchers (e.g. Baker et al., 1989 and 1991) have taken many of the costs of concurrent effects into account by evaluating the costs associated with the treatment of cancer patients in relation to medical costs of individuals without cancer (referred to as background medical costs). When background costs are subtracted from the total medical costs to cancer patients, the remaining incremental costs to cancer patients include costs of treating side effects, as well as the original cancer treatment costs. Baker et al.'s values are reported in Chapters II.2., II.3, II.4, II.5, II.7, and II.8.

This incremental approach captures medical costs associated with side effects that occur during treatment for the original cancer, but those that occur at a later date may not be included. For example, medical costs associated with a second cancer that occurs years later, induced by radiation therapy, would not be included using this approach. There are currently no very long-term follow-up data on these types of costs. This omission is likely to lead to an underestimate of total medical costs.

II.1.C. Causality and Special Susceptibilities

Carcinogens may act directly in causing cancer (initiators), or with other chemicals or individual characteristics to promote the development of cancer (promoters). Both initiators and promoters increase cancer risk. Cancer involves a change in cells that eliminates the normal controls on the growth of cells (Williams and Weisburger, 1993). Most carcinogens interact with DNA to alter the basic genetic directions of cells. Common characteristics of these carcinogens are that their effects are persistent, cumulative, and delayed (Ibid). The delay in effects, often for decades, make their identification and the quantification of their risks to humans difficult.

Although thousands of studies of the carcinogenicity of chemicals are conducted, most are carried out in animals due to:

1) the long delay after exposure in the development of tumors in humans, as noted above;

2) ethical issues;

3) costs of conducting human studies; and

4) difficulties with the confounding effects of carcinogens not under study.[1]

Animals are used because they provide a controlled set of subjects whose exposure can be measured accurately. Due to their relatively short life span, cancer can be observed and quantified in a reasonable amount of time in animals, especially in rodents. They are typically given large doses because this allows a relatively small number of animals to be used (e.g., 50 or 100) to obtain a statistically significant result. The results are then scaled to a human dose and response.

The chemical induction of cancer in animals is generally assumed to be evidence that the chemical may pose cancer risks to humans. EPA's *Proposed Guidelines for Cancer Risk Assessment* state that:

> "The default assumption is that positive effects in animal cancer studies indicate that the agent under study can have carcinogenic potential in humans. Thus if no adequate human data are present, positive effects in animal cancer studies are a basis for assessing the carcinogenic hazard to humans... The assumption is supported by the fact that nearly all of the agents known to cause cancer in humans are carcinogenic in animals in tests with adequate protocols... Further support is provided by research on the molecular biology of cancer processes, which has shown that the mechanisms of control of cell growth and differentiation are remarkably homologous among species..." (EPA 1996).

These proposed guidelines are very similar to those which have been in force for the last decade (EPA 1986).[2]

Although the assumption is made that cancer induction in animals may indicate cancer risk in humans, it is not assumed that cancer will occur in the same organ(s) in humans as in animals (EPA 1996). In addition, carcinogens often act non-specifically, being capable of acting on multiple organ systems throughout the body. Consequently, most cancer studies

[1] The absolute prohibition against exposure to non-beneficial chemicals (e.g., pharmaceuticals) that exists for humans does not exist for animals, and most chemicals of toxicological interest continue to be tested on animals. Ethical issues still persist, however, when animal studies are conducted, due to procedures that raise serious ethical concerns.

[2] Many specific criteria are used in determining whether a chemical is carcinogenic. See the proposed cancer guidelines for more information (EPA 1996).

cannot be used to determine the specific site where cancer is likely to occur in humans, but can be used to strongly suggest that a cancer risk exists.[3] Because positive cancer study results in animals may be relevant to many types of cancer in humans, the results of cancer studies in animals are listed in this introductory cancer chapter rather than in the individual cancer chapters that deal with a specific organ (e.g., kidney cancer, lung cancer).

II.1.D. Chemicals Associated with Cancer Induction

Table II.1-1 lists chemicals that have been associated with carcinogenic effects in either animal or human studies, based on EPA's review of the carcinogenicity data. The chemicals listed in Table II.1-1 have been identified as potential human carcinogens in one or more of EPA's large toxicity databases: HSDB, IRIS, or HEAST. The table, compiled in 1996, is *not* a comprehensive list of all carcinogens.

The chemicals listed in Table II.1-1 are a sample of the potential environmental agents associated with this disease. Although the table contains many chemicals, it is incomplete for two reasons:

1. It does not include toxicological data from sources other than HSDB, IRIS, and HEAST. The toxicological literature currently available is vast, and a thorough review was beyond the scope of this analysis.

2. Many chemicals have not been tested, or the results of the tests are inconclusive. Consequently, the human health effects of many environmental hazards are unknown, especially at concentrations found in the environment.

[3] When portal-of-entry effects or other location-specific interactions occur, cancer sites can be more specifically predicted.

Table II.1-1. SUSPECTED CARCINOGENS LISTED IN IRIS, HEAST, AND HSDB

Chemicals are listed alphabetically and TRI chemicals as of August 2000 are shown with an asterisk. When "compounds" of a metal were listed on TRI, all compounds of that metal in this table are considered to be TRI chemicals. See text for discussion of inclusion criteria. This is not a comprehensive list of all carcinogens.

CHEMICAL	SOURCE(S)
ACENAPHTHENE	HSDB
ACENAPHTHYLENE	HSDB
ACEPHATE*	IRIS
ACRYLAMIDE*	IRIS
ACRYLONITRILE*	HSDB, IRIS
ALACHLOR*	HEAST
ALDRIN*	IRIS
ALKANOLAMINE SALTS, 2,4-D,	HSDB
ALUMINUM*	HSDB
ALUMINUM FLUORIDE	HSDB
ALUMINUM OXIDE*	HSDB
ALUMINUM SODIUM FLUORIDE	HSDB
AMMONIUM CHROMATE	HSDB
AMMONIUM DICHROMATE	HSDB
AMOSITE	HSDB
AMPICILLIN	HSDB
ANILINE*	IRIS
ARAMITE	IRIS
ARSENIC*	HSDB, IRIS
ARSENIC ACID*	HSDB
ARSENIC PENTOXIDE*	HSDB
ARSENIC TRIBROMIDE*	HSDB
ARSENIC TRICHLORIDE*	HSDB
ARSENIC TRIIODIDE*	HSDB
ARSENIC TRIOXIDE*	HSDB
ARSENIC TRISULFIDE*	HSDB
ARSINE	HSDB
ASBESTOS*	HSDB
ASPHALT	HSDB
ATRAZINE*	HEAST
ATTAPULGITE	HSDB
AZOBENZENE	IRIS
BENZENE*	HSDB, IRIS
BENZENE HEXACHLORIDE	HSDB
BENZIDINE*	HSDB, IRIS
BENZO(A)PYRENE*	HSDB
BENZO(B)FLUORANTHENE*	HSDB
BENZOTRICHLORIDE	HSDB, IRIS
BENZOYL CHLORIDE*	HSDB
BENZO[A]PYRENE	IRIS
BENZYL CHLORIDE*	IRIS
BERYLLIUM*	HSDB, IRIS
BERYLLIUM CHLORIDE*	HSDB
BERYLLIUM FLUORIDE*	HSDB
BERYLLIUM HYDROXIDE*	HSDB
BERYLLIUM NITRATE*	HSDB
BERYLLIUM OXIDE*	HSDB
BERYLLIUM PHOSPHATE*	HSDB

Table II.1-1. SUSPECTED CARCINOGENS LISTED IN IRIS, HEAST, AND HSDB

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CHEMICAL	SOURCE(S)
BERYLLIUM SULFATE*	HSDB
BIS(2-CHLOROETHYL) ETHER*	HEAST
BIS(2-CHLOROETHYL)SULFIDE	HSDB
BIS(CHLOROETHYL)ETHER	IRIS
BIS(CHLOROMETHYL) ETHER*	HSDB, IRIS
BROMO-2-CHLORO-1,1,1-TRIFLUOROETHANE, 2-	HSDB
BROMOCHLORODIFLUOROMETHANE*	HSDB
BROMODICHLOROMETHANE	IRIS
BROMOETHENE (VINYL BROMIDE)*	HEAST
BROMOFORM*	IRIS
BUTADIENE, 1,3-*	HSDB
BUTYRIC ACID, 4-(2,4-DICHLOROPHENOXY)	HSDB
CALCIUM ARSENATE	HSDB
CALCIUM ARSENITE	HSDB
CALCIUM CHROMATE	HSDB
CAPTAFOL	HEAST
CAPTAN*	HEAST
CARBAZOLE	HEAST
CARBON BLACK	HSDB
CARBON TETRACHLORIDE*	HSDB, IRIS
CHLORAMBUCIL	HSDB
CHLORAMPHENICOL	HSDB
CHLORANIL	HEAST
CHLORDANE	HSDB, IRIS
CHLORO-1,1,1,2-TETRAFLUOROETHANE, 2-*	HSDB
CHLORO-1,3-BUTADIENE, 2-	HSDB
CHLORO-2-FLUOROETHANE, 1-	HSDB
CHLORO-2-METHYLANALINE, 4-	HEAST
CHLORO-2-METHYLANILINE HYDROCHLORIDE	HEAST
CHLORO-2-METHYLPHENOL, 4-	HSDB
CHLOROBENZILATE*	HEAST
CHLORODIFLUOROMETHANE*	HSDB
CHLOROFORM*	IRIS
CHLOROMETHANE*	HEAST
CHLOROMETHYL METHYL ETHER*	HSDB
CHLORONITROBENZENE, O-	HEAST
CHLORONITROBENZENE, P-	HEAST
CHLOROPENTAFLUOROETHANE	HSDB
CHLOROTETRAFLUOROETHANE	HSDB
CHLOROTHALONIL	HEAST
CHROMIC ACID, CHROMIUM(3+) SALT	HSDB
CHROMIC OXIDE	HSDB
CHROMIC SULFATE	HSDB
CHROMIC TRIOXIDE	HSDB
CHROMITE	HSDB
CHROMIUM*	HSDB
CHROMIUM CHROMATE*	HSDB
CHROMIUM DIOXIDE*	HSDB
CHROMIUM TRIHYDROXIDE*	HSDB
CHROMIUM(III) ACETATE*	HSDB
CHROMOUS CHLORIDE	HSDB

Table II.1-1. SUSPECTED CARCINOGENS LISTED IN IRIS, HEAST, AND HSDB

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CHEMICAL	SOURCE(S)
CHROMOUS OXALATE	HSDB
CHROMYL CHLORIDE	HSDB
CHRYSOTILE ASBESTOS	HSDB
CIS-DIAMINEDICHLOROPLATINUM	HSDB
CLOMIPHENE	HSDB
CLOZARIL	HSDB
COAL TAR USP	HSDB
COAL TAR CREOSOTE*	HSDB
COAL TAR	HSDB
COPPER*	HSDB
CREOSOTE, WOOD*	HSDB
CYANAZINE*	HEAST
CYCLOPHOSPHAMIDE	HSDB
D, 2,4-*	HSDB
D BUTOXYETHYL ESTER, 2,4-*	HSDB
D, BUTOXYPROPYL ESTER, 2,4-*	HSDB
D BUTYL ESTER, 2,4-*	HSDB
D CHLOROCROTYL ESTER, 2,4-*	HSDB
D, DIMETHYLAMINE, 2,4-*	HSDB
D ISOOCTYL ESTERS, 2,4-*	HSDB
D ISOPROPYL ESTER, 2,4-*	HSDB
D, PROPYLENE GLYCOL BUTYL ETHER ESTER, 2,4-*	HSDB
DAUNORUBICIN	HSDB
DDT	HSDB
DI(2-ETHYLHEXYL)ADIPATE	IRIS
DI(2-ETHYLHEXYL)PHTHALATE*	IRIS
DIALLATE*	HEAST
DIBENZ(A,H)ACRIDINE*	HSDB
DIBENZ(A,J)ACRIDINE*	HSDB
DIBENZO(A,E)PYRENE*	HSDB
DIBENZO(A,H)PYRENE*	HSDB
DIBENZO(A,L)PYRENE*	HSDB
DIBENZO(C,G)CARBAZOLE, 7H-*	HSDB
DIBROMO-3-CHLOROPROPANE, 1,2*	HEAST
DIBROMOCHLOROMETHANE	IRIS
DIBROMOETHANE, 1,2-*	IRIS
DIBROMOTETRAFLUOROETHANE, 1,2-	HSDB
DICHLORFOP-METHYL	HSDB
DICHLORO-1,1,2-TRIFLUOROETHANE*	HSDB
DICHLORO-1,1,1-TRIFLUOROETHANE, 2,2-*	HSDB
DICHLORO-1,1,2,2-TETRAFLUOROETHANE, 1,2-	HSDB
DICHLORO-1,1-DIFLUOROETHANE, 1,2-*	HSDB
DICHLORO-1-FLUOROETHANE, 1,1-*	HSDB
DICHLORO-2-BUTENE, 1,4-*	HEAST
DICHLOROBENZENE*	HSDB
DICHLOROBENZENE, 1,4-*	HSDB
DICHLOROBENZENE, 1,2-*	HSDB
DICHLOROBENZENE, 1,3-*	HSDB
DICHLOROBENZENE, 1,4-*	HEAST
DICHLOROBENZIDINE, 3,3'-*	HSDB, IRIS
DICHLORODIFLUOROMETHANE*	HSDB

Table II.1-1. SUSPECTED CARCINOGENS LISTED IN IRIS, HEAST, AND HSDB

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CHEMICAL	SOURCE(S)
DICHLORODIPHENYL DICHLOROETHANE, P,P'-	IRIS
DICHLORODIPHENYLDICHLOROETHYLENE, P,P'-	IRIS
DICHLORODIPHENYLTRICHLOROETHANE, P,P'-	IRIS
DICHLOROETHANE, 1,2-*	IRIS
DICHLOROETHYLENE, 1,1-	IRIS
DICHLOROMETHANE*	HSDB, IRIS
DICHLOROPHENOL, 2,4-*	HSDB
DICHLOROPROPANE, 1,2-*	HEAST
DICHLOROPROPENE, 1,3-	HSDB
DICHLOROTRIFLUOROETHANE*	HSDB
DICHLORVOS*	HSDB, IRIS
DIELDRIN	IRIS
DIENESTROL	HSDB
DIETHYLSTILBESTROL	HEAST
DIMEHTYLBENZIDINE, 3,3-*	HEAST
DIMETHOXYBENZIDINE, 3,3-*	HEAST
DIMETHYL SULFATE*	HSDB
DIMETHYLANALINE HYDROCHLORIDE, 2,4-	HEAST
DIMETHYLANILINE, 2.4-	HEAST
DIMETHYLCARBAMOYL CHLORIDE*	HSDB
DINITROTOLUENE MIXTURE, 2,4-/2,6-*	IRIS
DIOXANE, 1,4-*	IRIS
DIPHENYLHYDRAZINE, 1,2-*	IRIS
DIRECT BLACK 38*	HEAST
DIRECT BLUE 6*	HEAST
DIRECT BROWN *95	HEAST
EPICHLOROHYDRIN*	HSDB, IRIS
ESTRONE	HSDB
ETHANOL	HSDB
ETHYL ACRYLATE*	HEAST
ETHYL CARBAMATE	HSDB
ETHYLENE GLYCOL DINITRATE	HSDB
ETHYLENE OXIDE*	HEAST, HSDB
ETHYLENE THIOUREA*	HEAST
FERRIC ARSENATE	HSDB
FERRIC OXIDE	HSDB
FERROUS ARSENATE	HSDB
FLUOROURACIL*	HSDB
FOLPET*	IRIS
FOMESAFEN*	IRIS
FORMALDEHYDE*	HSDB
FURAZOLIDONE	HEAST
FURIUM	HEAST
FURMECYCLOX	IRIS
GASOLINE	HSDB
GILSONITE	HSDB
HCFC-123A *	HSDB
HCFC-123B*	HSDB
HCFC-124A*	HSDB
HEMATITE	HSDB
HEPTACHLOR*	HSDB, IRIS

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CHEMICAL	SOURCE(S)
HEPTACHLOR EPOXIDE	IRIS
HEXACHLOROBENZENE*	IRIS
HEXACHLOROBUTADIENE	IRIS
HEXACHLOROCYCLOHEXANE, ALPHA-	IRIS
HEXACHLOROCYCLOHEXANE, BETA-	IRIS
HEXACHLOROCYCLOHEXANE, GAMMA-	HEAST
HEXACHLOROCYCLOHEXANE, TECHNICAL	IRIS
HEXACHLORODIBENZO-P-DIOXIN*	IRIS
HEXACHLOROETHANE*	IRIS
HEXAHYDRO-1,3,5-TRINITRO-1,3,5-TRIAZINE	IRIS
HYDRAZINE*	HSDB
HYDRAZINE/HYDRAZINE SULFATE*	IRIS
ISOPHORONE	IRIS
KEROSENE	HSDB
LEAD ARSENATE*	HSDB
LEAD CHROMATE*	HSDB
LEAD PHOSPHATE*	HSDB
LITHIUM CHROMATE	HSDB
MAGNESIUM ARSENATE	HSDB
MECHLORETHAMINE	HSDB
MELPHALAN	HSDB
MERCURY, ELEMENTAL*	HEAST
METHALLENESTRIL	HSDB
METHOXSALEN	HSDB
METHOXY-5-NITROANILINE, 2-	HEAST
METHOXYPSORALEN, 5-	HSDB
METHYL ISOBUTYL KETONE*	HSDB
METHYL-5-NITROANILINE, 2-	HEAST
METHYLANILINE, 2-	HEAST
METHYLANILINE HYDROCHLORIDE, 2-	HEAST
METHYLENE BIS(N,N'-DIMETHYL)ANILINE, 4,4'-	IRIS
MOLYBDATE ORANGE	HSDB
NAPHTHYLAMINE, 2-	HSDB
NICKEL*	HSDB
NICKEL CARBONATE*	HSDB
NICKEL CARBONYL*	HSDB
NICKEL CHLORIDE*	HSDB
NICKEL FORMATE*	HSDB
NICKEL HYDROXIDE*	HSDB
NICKEL OXIDE*	HSDB
NICKEL SULFATE*	HSDB
NITROFURAZONE	HEAST
NITROPROPANE, 2-*	HEAST
NITROQUINOLINE-N-OXIDE, 4-	HSDB
NITROSO-DI-N-BUTYLAMINE, N-*	IRIS
NITROSO-M-ETHYLUREA, N-	HEAST
NITROSO-N-METHYLETHYLAMINE, N-	IRIS
NITROSODI-N-PROPYLAMINE, N-*	IRIS
NITROSODIETHANOLAMINE, N-	IRIS
NITROSODIETHYLAMINE, N-**	IRIS
NITROSODIMETHYLAMINE, N-*	IRIS

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CHEMICAL	SOURCE(S)
NITROSODIPHENYLAMINE, N-*	IRIS
NITROSOPYRROLIDINE, N-	IRIS
OCHRATOXIN A	HSDB
ORYZALIN*	HSDB
OXYPHENBUTAZONE	HSDB
PENTABROMO-6-CHLOROCYCLOHEXANE, 1,2,3,4,5-	HEAST
PENTACHLORONITROBENZENE	HEAST
PENTACHLOROPHENOL*	HSDB, IRIS
PENTACHLOROPHENOL, SODIUM SALT*	HSDB
PETROLEUM ETHER	HSDB
PHENOBARBITAL	HSDB
PHENYLBUTAZONE	HSDB
PHENYLENEDIAMINE, O-	HEAST
PHENYLPHENOL, 2-*	HEAST
POLYBROMINATED BIPHENYLS*	HEAST
POLYCHLORINATED BIPHENYLS*	IRIS
POLYVINYL CHLORIDE	HSDB
POTASSIUM ARSENATE	HSDB
POTASSIUM ARSENITE	HSDB
PROCHLORAZ	IRIS
PROPIONIC ACID, 2-(3-CHLOROPHENOXY)	HSDB
PROPYL THIOURACIL	HSDB
PROPYLENE OXIDE*	IRIS
QUINOLINE*	HEAST
RADIUM	HSDB
RADON	HSDB
SILICON DIOXIDE	HSDB
SIMAZINE*	HEAST
SODIUM ARSENATE	HSDB
SODIUM ARSENITE	HSDB
SODIUM CHROMATE	HSDB
SODIUM DICHROMATE	HSDB
SODIUM DIETHYLDITHIOCARBAMATE*	HEAST
STREPTOZOTOCIN	HSDB
STRONTIUM	HSDB
STRONTIUM CHROMATE	HSDB
T, 2,4,5-	HSDB
TALC	HSDB
TETRACHLORODIBENZO-P-DIOXIN, 2,3,7,8- *	HSDB, HEAST
TETRACHLOROETHANE, 1,1,1,2-*	IRIS
TETRACHLOROETHANE, 1,1,2,2-*	IRIS
TETRACHLOROPHENOL, 2,3,4,6-	HSDB
TETRACHLOROTOLUENE, PARA, ALPHA, ALPHA, ALPHA-	HEAST
TETRACHLOROVINPHOS/(STIROFOS)	HEAST
TETRAETHYL LEAD	HSDB
THIO-TEPA	HSDB
THORIUM DIOXIDE*	HSDB
TITANIUM DIOXIDE	HSDB
TOLUENE-2,4-DIAMINE	HEAST
TOLUIDINE, P-	HEAST
TOXAPHENE*	HSDB, IRIS

Table II.1-1. SUSPECTED CARCINOGENS LISTED IN IRIS, HEAST, AND HSDB

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CHEMICAL	SOURCE(S)
TP, 2,4,5-	HSDB
TREMOLITE ASBESTOS	HSDB
TRICHLOROANILINE, 2,4,6-	HEAST
TRICHLOROANILINE HYDROCHLORIDE, 2,4,6-	HEAST
TRICHLOROETHANE, 1,1,2-*	IRIS
TRICHLOROFLUOROMETHANE*	HSDB
TRICHLOROPHENOL, 2,4,5-*	HSDB
TRICHLOROPHENOL, 2,4,6-*	IRIS
TRICHLOROPROPANE, 1,2,3-	HEAST
TRIFLURALIN*	IRIS
TRIMETHYL PHOSPHATE	HEAST
TRINICKEL DISULFIDE	HSDB
TRINITROTOLUENE, 2,4,6-	IRIS
URANIUM	HSDB
URANYL ACETATE	HSDB
URANYL NITRATE	HSDB
URANYL SULFATE	HSDB
VINCRISTINE	HSDB
VINYL CHLORIDE*	HEAST, HSDB
VITAMIN A	HSDB
ZINC CHROMATE*	HSDB
ZINC CHROMATE HYDROXIDE*	HSDB
ZINC DICHROMATE*	HSDB
ZINC POTASSIUM CHROMATE*	HSDB

For these reasons, Table II.1-1 should not be used as a definitive source of information on the links between chemicals and cancer. A comprehensive literature search is necessary to identify the dose-response relationships between chemicals of concern and this or other health effects.

The chemicals with asterisks in Table II.1-1 are TRI chemicals (subject to reporting under the Toxics Release Inventory, Section 313 of the Emergency Planning and Community Right-to-Know Act). When "compounds" of a metal were listed on TRI, all compounds of that metal in this table are considered to be TRI chemicals. Chemicals included on the TRI due to their human health effects are known or reasonably anticipated to cause either significant adverse acute health effects or chronic health effects as a condition of their listing on TRI.

The route of exposure (e.g., oral, inhalation, dermal) is often considered when evaluating whether a chemicals poses a carcinogenic risk. The routes of exposure are not listed in Table II.1-1 for two reasons:

1. A chemical that is carcinogenic by one route of exposure will usually be assumed to be carcinogenic by other routes of exposure. EPA's proposed cancer guidelines state that it is assumed "that an agent that causes internal tumors by one route of exposure will be carcinogenic by another route if it is absorbed by the second route to give an internal dose" (EPA 1996). In effect, most carcinogens will fall under this assumption under most circumstances.

2. This table provides preliminary information on many chemicals identified as potential human carcinogens. Risk or health assessment, however, requires considerably more information than that provided in the table. Consequently, additional information must be collected and evaluated by researchers to fully evaluate cancer risks; an analysis of route-specific data is a part of this evaluation.

In considering the potential impacts of carcinogens, it is useful to note that a number of them are known to cross the placental barrier, and some cancers are likely to be the result of this type of exposure (Williams and Weisburger,1993).

II.1. E. Genotoxicity

Genotoxicity assays usually provide information regarding a chemical's ability to interact with DNA. Genotoxicity may be associated with cancer induction because, in most cases, the alteration in the cells' normal replication methods allows uncontrolled growth that characterizes cancer. Table II.1-2 contains a listing of chemicals associated with genotoxic effects listed in a variety of sources.[4] These chemicals have yielded positive results in genotoxicity assays, which are usually cell-level studies of a chemical's interaction with the genetic material (DNA) within a cell and/or its ability to cause mutations. Genotoxins are not all necessarily carcinogenic to humans; however, genotoxicity indicates the potential for actions that may cause cancer. Table II.1-2 contains only a small percentage of all the chemicals that have had positive genotoxicity assays. As of 1990, the Environmental Mutagen Information Center in Oak Ridge, Tennessee, maintained mutagenicity data on 21,000 chemicals (Hoffmann,1991). The size of the database indicates the magnitude of the chemicals of potential interest regarding their carcinogenic capabilities.[5]

[4] Table II.1-1 contains both genotoxic and non-genotoxic carcinogens with the criteria for inclusion being a positive carcinogenicity assay. A positive genotoxicity assay was the criterion for inclusion in Table II.1-2.

[5] Not all carcinogens are genotoxic (e.g., hormonally-mediated carcinogens). See EPA (1996) for a discussion of this distinction.

Chapter III.1 contains an additional discussion of genotoxicity relevant to birth defects.

Link to III.I.C.4

Table II.1-2. CHEMICALS ASSOCIATED WITH GENOTOXIC EFFECTS
DATA FROM HUMAN, ANIMAL, AND IN VITRO STUDIES ARE INCLUDED.

CHEMICAL	REFERENCES
ACETONE*	5
ACROLEIN*	4
ACRYLIC ACID*	7
ACRYLONITRILE*	5
ALACHLOR*	1
ALDICARB*	1
AMINOPTERIN	3
AMITRAZ*	6
AMITROLE*	5
ANTU	5
AROCLOR 1016 (A PCB)*	7
ARSENIC COMPOUNDS*	6
ARSENIC*	6
ASULAM	7
ATRAZINE*	9
AVERMECTIN B1	7
BENOMYL *	1,7
BENZENE*	5
BENZO(A)PYRENE*	14
BIORESMETHRIN	1
BISULFAN	14
BORIC ACID	5
BRADIFACOUM	1
BUSULFAN	3
BUTACHLOR	4
CADMIUM*	14
CAPROLACTAM	7
CAPTAFAL	6
CAPTAN*	7,6
CARBARYL*	6
CARBOFURAN*	6
CARBON TETRACHLORIDE*	1
CARBON DISULFIDE*	5
CARBOPHENOTHION	1
CHLORDANE*	12
CHLORDECONE	1
CHLORDIMEFORM	6
CHLORFENVINPHOS	6
CHLORMEQUAT	5
CHLOROBENZILATE*	7
CHLOROBIPHENYLS (INCLUDES PCBS)*	3
CHLOROFORM*	1
CHLOROPHACINONE	1
CHLOROPROPHAM	7
CHLOROTHALONIL*	1
CHLORPROPHONE	1
CHROMIUM*	16
COPPER SULFATE*	5

Table II.1-2. CHEMICALS ASSOCIATED WITH GENOTOXIC EFFECTS
DATA FROM HUMAN, ANIMAL, AND IN VITRO STUDIES ARE INCLUDED.

CHEMICAL	REFERENCES
COUMACHLOR	1
COUMAFURYL	1
COUMATETRALYL	1
CYANIDES*	1
CYCLOHEXANE*	5
CYCLOHEXANONE	5
CYCLOHEXIMIDE	5
CYCLOPENTAPYRENE	2
CYCLOPHOSPHAMIDE	14
CYHALOTHRIN*	7
2,4-D*	6
DALAPON	5
DECAMETHRIN	1
DEET (DIETHYLTOLUAMIDE)	5
DI(2-ETHYL HEXYL) ADIPATE	7
DIBROMOCHLOROPROPANE*	5,6
DICAMBA*	7
DICHLOBENIL	1
O-DICHLOROBENZENE*	1
P-DICHLOROBENZENE*	5
DICHLOROETHYL ETHER	5
1,3-DICHLOROROPENE (2,3 ON TRI)	5
DICHLORVOS*	13
DIETHYLSTILBESTROL (DES)	3
DIFENACOUM	1
DIMETHOATE*	6
DIMETHYL SULFOXIDE	5
DINOSEB	14
DIOXANE *	5
DIPHACINONE	1
DIPHENYLHYDANTOIN	3
DIQUAT	5
DISULFOTON	1
DIURON*	5
ENDRIN	6
EPICHLOROHYDRIN*	5
EPN	1
EPTC	7
ETHANOL	14
ETHYL BENZENE *	
ETHYLENE DIBROMIDE	8,6
ETHYLENE DICHLORIDE*	5
ETHYLENE THIOUREA*	14
ETHYLENE OXIDE*	5
ETHYLNITROSUREA	3
EUGENAL	5
FENBUTATIN OXIDE*	1
FERBAM*	1
FLUOMETURON*	6
FLURPRIMIDOL	7
FLUTOLANIL	7
FOLPET*	8
FORMALDEHYDE*	5
GLYCEROL FORMAL	1

Table II.1-2. CHEMICALS ASSOCIATED WITH GENOTOXIC EFFECTS
DATA FROM HUMAN, ANIMAL, AND IN VITRO STUDIES ARE INCLUDED.

CHEMICAL	REFERENCES
GLYPHOSATE	7
HALOXYFOP METHYL	7
HEXACHLOROBENZENE*	5
HEXACHLOROPHENE*	1
LEAD*	14
LINDANE*	1
LINURON*	5
LITHIUM (TRI LISTED AS LITHIUM CARBONATE)*	3
MALATHION*	1
MALEIC HYDRAZIDE*	5
MANEB*	6
MCPA*	1
MERCURY*	7
MERCURY COMPOUNDS*	15
METALDEHYDE	5
METHIDATHION	1
METHIMAZOLE	3
METHOMYL	6
METHOXYCHLOR*	5,7
METHYL ETHYL KETONE (MEK) *	7
METHYL BROMIDE	1
METHYL METHACRYLATE*	5
METHYLCHOLANTHRENE*	14
METHYLENE CHLORIDE	5
METOLACHLOR	1,7
MEXACARBATE	1
MIREX	14
MNNG	3
MOLINATE*	1
NABAM*	5
NAPHTHALENES*	1
NAPROPAMIDE	7
NICKEL*	15
NICOTINES*	1
NITRATE*	7
NITRITE	7
NITROFEN*	4
NITROGUANIDINE	7
OXYFLUORFEN*	6
PARAQUAT*	5
PARATHION*	1
PCBS*	
PENTACHLORONITROBENZENE	1
PENTACHLOROPHENOL*	1
PERCHLOROETHYLENE*	1
PERMETHRIN*	1
PHENMEDIPHAM	1
PHENOL*	1,7
O-PHENYLPHENOL*	5
PHOSMET	1
PICLORAM*	1
PIDRIN	7
PINDONE	1
PIPERONYL BUTOXIDE*	1

Table II.1-2. CHEMICALS ASSOCIATED WITH GENOTOXIC EFFECTS
DATA FROM HUMAN, ANIMAL, AND IN VITRO STUDIES ARE INCLUDED.

CHEMICAL	REFERENCES
PIRIMICARB	1
PIRIMIPHOS-ETHYL	1
PIRIMIPHOS-METHYL*	6
2-PIVALYL-1,3 INDANDIONE	1
PROPACHLOR*	4
PROPARGITE*	7
PROPHAM	1
PROPOXUR*	1
PROPYLENE OXIDE*	5
PROPYLENE DICHLORIDE	5
PYRAZON	1
PYRIDINE*	5
RADIONUCLIDES (ALPHA, BETA, & GAMMA EMITTERS)	3
RESMETHRIN*	7
RONNEL	1
ROTENONE	1
SODIUM CHLORATE	5
STRYCHNINE*	5
SULFUR DIOXIDE	5
TCDD	14
2,4,5-T	1
2,4,5-TP	1
TETRACHLORVINPHOS*	1
TETRACYCLINES	3
THIABENDAZOLE*	5
THIOPHANATE-METHYL 6*	6
THIRAM*	1
TOLUENE*	5
TOXAPHENE*	6
TRICHLORFON*	13
1,2,4-TRICHLOROBENZENE*	7
1,1,1-TRICHLOROETHANE*	5
TRICHLOROETHYLENE*	5
TRIDIPHANE	7
TRIFLURALIN*	6
TRIFORINE*	1
TRIMETHADONE	3
URETHANE*	14
VALPROIC ACID	3
VERNAM	7
WARFARIN*	1
WHITE PHOSPHORUS*	
XYLENE*	5
ZINEB*	5
ZIRAM	1

Table II.1-2. CHEMICALS ASSOCIATED WITH GENOTOXIC EFFECTS
DATA FROM HUMAN, ANIMAL, AND IN VITRO STUDIES ARE INCLUDED.

* = Listed in TRI as of August 2000 . When "compounds" of a metal were listed on TRI, all compounds of that metal in this table are considered to be TRI chemicals

References

1. Cunningham and Hallenbeck (1985).
2. Archer and Livingston (1983).
3. Doull et al .(1980).
4. U.S. EPA 1983).
5. U.S. Department of Health and Human Services, NIOSH (1983).
6. U.S. EPA (1983).
7. IRIS, U.S. EPA online database.
8. Clayton and Clayton (1982).
9. Hayes (1982).
10. Vettorazzi (1979).
11. Council on Environmental Quality (1981).
12. International Agency for Research on Cancer (1979).
13. Chambers and Yarbrough (1982)
14. Key et al. (1977).
15. Tice et al. (1996).
16. U.S. Department of Health and Human Services, ATSDR (1993).

II.1.F. Selection of Diseases

The selection of cancers included in this section was based on input from a variety of sources (as discussed in Chapter I.1). It is anticipated that additional cancers will be added in the future.

Link to Chapter I.1

II.1.G. Prognosis

II.1.G.1 General Issues

Cancers vary widely in the course of the diseases. Some types of cancer have a relatively good prognosis (e.g., non-Hodgkins lymphoma), with most patients surviving the course of the disease. Others, such as lung cancer, are much more often fatal. Although generalizations can be made regarding the "average" prognosis for each cancer, the prognosis for survival and the length of time over which treatment is required vary among individuals, even for the same type of cancer. This variability is observed for all types of cancer. Consequently, the cost estimates presented in the chapters in this section utilize estimates of the average survival rates to obtain representative estimates of the medical costs.

In addition to the individual variability in survival, patterns in survival for specific types of cancer are based on patient characteristics. For example, elderly patients with breast cancer typically have slower tumor growth than younger patients. There may also be differences related to gender and race. Although this type of pattern evaluation was beyond the scope of this handbook, it may have an impact on the cost of medical treatment. (When information was available in texts reviewed for other purposes, survival patterns are reported.) Consequently, if an analysis is being conducted on a homogeneous population (similar age, ethnicity, etc.), then it is advisable to survey the literature to determine if patterns in disease course or survival exist that may be relevant to an economic evaluation.

II.1.G.2 Survival Estimates

It is often important to obtain estimates of survival and mortality that are as accurate as possible because medical costs depend on the duration of treatment and whether patients are survivors or nonsurvivors. For example, the value of a statistical life may be used for nonsurvivors, whereas the summed direct medical and other costs may be used for survivors. Obtaining accurate estimates of mortality due to a disease is difficult unless the disease has a very short duration prior to death.[6] When the illness is protracted, as it is for most cancers, it is necessary to evaluate multiple years of vital statistics for patients to obtain reliable mortality estimates. For many illnesses there are scant data of this type; however, the National Cancer Institute (NCI) maintains this data for most cancers through their Surveillance, Epidemiology, and End Results (SEER) Program and database, which is available both on line and in documents published through the Biometry Branch of NCI.

Survival and mortality data are reported in SEER as the Relative Survival Rate (RSR) for each cancer for each year post-diagnosis. It is usually reported for the years 1973 to 1993, but for rare cancers may only be provided for five years post-diagnosis. The stomach cancer chapter in this handbook contains a detailed discussion of RSRs, and their derivation. They are statistics based on the survival of cancer patients in relation to the general population of the same age (hence the term “relative”). For purposes of determining the percent of patients who are survivors and nonsurvivors, a complex process that is described in the stomach cancer chapter can be used to obtain a precise estimate of these percents. For most uses, however, the RSRs provide a sufficiently close approximation

[6] Mortality here refers to the risk that death will occur due to the illness under study, and can be expressed as a rate (e.g., the percentage of all patients who ultimately die of the disease).

of survival and mortality percents to be used without modification. An example of a simplified approach to survival estimates is provided in the discussion of bone and liver cancer in this chapter (Section II.1.H.6.4).

Links to Chapter II.2 for detailed discussion of RSRs and Section II.1.H.6.4

II.1.H Typical Cancer Costs

Although cancer costs among individuals vary widely, there are similarities in the average costs reported for cancers. This section reports and analyzes some of these costs. The data in this section may be useful when evaluating a cancer for which cost data aren't available (e.g., a rare cancer such as bone cancer), or when the specific type of cancer is not known but a cancer risk is projected (i.e. from an animal study) and a typical value is sought.

The cost estimate provided in this section is referred to as a "typical cancer" cost rather than an average cost because it is not a statistical average of all cancer costs. Rather, the estimate is based on the average cost calculated from the only long-term study of cancer costs available (Baker et al., 1989). The costs reported here cannot be represented as average costs because they are not based on an average of either all cancers or a random sample of cancers. Cost estimates are based on a group of cancers that represent the vast majority of cancers that occur in the U.S., however, and so offer a reliable estimate of typical costs.

II.1.H.1. Source

The most recent source located for lifetime direct medical costs of a number of cancers is Baker et al. (1989). Baker et al. evaluated the continuous Medicare history sample file (CMHSF) from the Health Care Financing Administration. The file contains a random sample of five percent of all Medicare beneficiaries enrolled in 1974 in the United States, and includes all Medicare activity from 1974 to 1981. They chose CMHSF because:

1) it is a nationally representative sample of the Medicare population (five percent), covering over 1.6 million patients;
2) it is longitudinal, dating from 1974 to 1981; and
3) it captures the majority of medical expenses for each beneficiary.

Five Medicare files are included in the CMHSF, which cover:
1) inpatient hospital stays,
2) skilled nursing facility stays,
3) home health agency charges,

4) physicians' services, and
5) outpatient and other medical services.[7]

Because CMHSF provides no indication of initial diagnosis, Baker et al. assumed that disease onset occurred when a diagnosis of cancer was listed on a hospitalization record following a minimum of one year without a cancer diagnosis. This assumption is reasonable due to the high frequency of hospitalization associated with these diseases (i.e., individuals diagnosed with cancer would usually be hospitalized).[8]

Baker et al. assigned costs associated with each cancer to three post-diagnostic time periods:

- initial treatment, during the first three months following diagnosis;
- maintenance care, between initial and terminal treatment; and
- terminal treatment during the final six months prior to death.

Initial treatment includes all diagnostic work, and any treatments provided in the first three months after diagnosis. This treatment may include radiation therapy, surgery, antineoplastic drugs, etc. Terminal care includes care provided only in the last six months of life. The care may be palliative or aggressive in nature and covers the spectrum of all potential cancer treatments. Maintenance care is defined as that care provided between the initial care phase and terminal treatment (for nonsurvivors) or cessation of care (for survivors). Maintenance includes any care provided after the first three months, excluding terminal care. It may include surgery, continued aggressive treatment with radiation or chemotherapy, diagnostics to determine the patient's progress, or be limited to ongoing monitoring and preventive therapies in cases where the cancer has been minimized or eliminated.

II.1.H.2. Modifications to the Data

There are a number of limitations to using Medicare data; these were addressed by Baker et al. with a variety of strategies. As noted in Chapter I.1, the amount paid for service may differ from the actual medical costs because many insurers and federal programs either 1) pay only a portion of

[7] See Baker et al. (1989 and 1991) for further details.

[8] Although there are some exceptions to this generalization, such as non-melanoma type skin cancers, very few cancers exist for which hospitalization is not required. (Medical costs for non-melanoma skin cancers are provided in this handbook in Chapter II..6)

Link to Chapter II.6

total costs or 2) pay more than actual costs to underwrite the care providers' losses due to underpayment from other sources. Baker et al. used provider charges, rather than Medicare reimbursements (which represent only a portion of most total charges), thus providing a more accurate cost estimate.

Link to Chapter I-1

To improve the accuracy of the cost estimates, Baker et al. included the costs of coinsurance, deductibles, and other cost components. They made four adjustments to the cost estimates calculated from the CMHSF:

- First, charges were added for skilled nursing facilities (SNFs) not covered by Medicare by multiplying the "length of stay" at an SNF (computed from admission and discharge dates) by the average daily SNF charge.

- Second, the annual Medicare Part B deductible of $60 was added to the reimbursed charges in the database.

- Third, since Medicare pays only 80 percent of physicians' charges, Baker et al. scaled these reimbursements to 100 percent of physicians' charges to better reflect costs.

- Finally, they inflated all dollar values to 1984 dollars using the Medical Care component of the Consumer Price Index.

Costs that were not included are outpatient prescription medications and nursing home care below the skilled level. The Mor et al. (1990) analysis of the CMHSF data notes that including costs incurred only after the initial diagnosis omits costs associated with prediagnostic tests and treatment. Although these costs could be significant, substantial medical treatment (e.g., tests requiring hospitalization) would also likely result in a diagnosis and thus be included in Baker et al.'s estimates. This omission may lead to an underestimate of costs by Baker et al. It is not likely to be substantial when viewed in the context of the overall costs of treatment.

II.1.H.3. Total Non-incremental Costs of Treatment Phases

Costs were evaluated for initial care and for each year post-diagnosis (i.e., the patient may have been in any year post-diagnosis to be included in the analysis). Patients with an initial diagnosis of cancer prior to or during the 1974 to 1981 time period numbered 125,832. Thirteen types of cancer had sufficient Medicare beneficiaries (more than 1,000) to be analyzed.

Table II.1-3 lists the cancer types; the number of patients diagnosed; and the costs of initial, maintenance, and terminal phases of care in 1984

dollars. As Table II.1-3 shows, there is a relatively small variation in costs among the cancers. Initial care costs vary by approximately a factor of 2, continuing care by a factor of approximately 1.8, and terminal care by a factor of approximately 1.3.

Table II.1-3 Cancer Types, Number of Study Subjects and Treatment Phase Costs[a]

		Treatment Phase Costs in 1984 Dollars[b]		
Cancer Type (ICD9 Code)	**# Patients**	**Initial**	**Maintenance (per year)**	**Terminal**
Colorectal (153-154)	19,673	$14,190	$572	$15,776
Lung (162)	15,381	$12,916	$690	$15,565
Prostate (185)	14,002	$8,112	$560	$14,613
Breast (174)	12,486	$7,606	$483	$15,136
Bladder (188)	6,843	$8,470	$766	$18,577
Leukemia (204-208)	3,740	$9,068	$676	$19,777
Pancreas (157)	3,231	$14,009	$677	$14,790
Stomach (151)	3,228	$14,443	$660	$16,132
Uterine corpus (182)	3,042	$9,260	$424	$17,623
Kidney (189)	1,953	$12,608	$670	$19,302
Ovary (183)	1,605	$11,055	$647	$18,650
Uterine cervix (180)	1,448	$8,979	$493	$16,414
Melanoma (172)	1,105	$6,954	$488	$16,194
Mean Costs		$10,590	$600	$16,811

a. Based on Baker et al., 1989. These are non-incremental and not discounted.
b. See text for definitions of treatment phases.

II.1.H.4. Maintenance Phase Costs

One complicating factor in evaluating cancer costs using the Baker et al. data is determining a value for maintenance care. As Table II.1-3 shows, this value is reported as a yearly cost. The duration of maintenance care for each cancer is not provided by the authors. It should be noted that maintenance care refers to a time period rather than to the nature of the care, and may include diagnostic tests, surgery, care during relapses, etc., and any other care provided more than three months after diagnosis and more than six months prior to death due to the cancer (but not due to other causes). Consequently, costs of maintenance care can vary widely among patients. It may occur for only a few months or for decades, due to variations in human disease patterns, disabilities, etc.

A variety of strategies can be used to estimate an average maintenance period. The most precise would be to determine the average length of maintenance care for survivors and non-survivors of different ages, either from the literature or through a national survey of medical practitioners for each type of cancer. Literature has not been located with statistics on maintenance care durations, and a survey of practitioners would be time-consuming, expensive, and have considerable uncertainty. It would be necessary to ascertain both how long a patient would be expected to live (for both survivors and non-survivors) and how long they would receive care if they lived for an extended time period. Some patients would not live as long as the "recommended" period of maintenance care, due to either death from cancer or from some other cause (i.e., background mortality). The typical cancer costs estimated in this section are to be used primarily for rare cancers that lack data; consequently, the necessary information on mortality and care is not generally available.

Given the unknowns, some simplifying assumptions were made to estimate maintenance costs for purposes of this "typical cancer" analysis. Rather than evaluate maintenance care for each cancer separately, an average duration of care was selected and an average cost calculated. Two simplifying assumptions were used:

1) It was assumed that the average patient (survivors and nonsurvivors combined) receives five years of maintenance care post-diagnosis.

2) Terminal costs were assumed to be applicable to 50 percent of patients (a 50 percent mortality rate); survival actually varies widely by cancer type.

Many patients will survive beyond the five-year maintenance period assumed in this analysis and continue to incur cost due to diagnostic tests, drugs, etc.[9] Five years, however, is a reasonable estimate for follow-up when non-survivors are included. Most cancers have a relatively high mortality rate, as reflected in the 50 percent mortality rate used as an assumption in this analysis. As a result of the two assumptions listed above, the average maintenance cost for five years was added to the initial costs plus one half of the terminal costs to obtain an estimate of the total cost.

[9] For example, the average age of diagnosis for most cancers is about 70 years. At this age the average member of the general population has a life expectancy of 14 years. Patients may incur additional costs over the full course of their lifespan.

II.1.H.5. Incremental Costs of Treatment Phases

The costs shown in Table II.1.3 are *all* medical costs incurred by a patient with a cancer diagnosis. Consequently, the costs must be adjusted for background medical expenses to obtain the incremental costs of cancer treatment. Baker et al. (1991) provides an estimated background cost per year of $2,988 (in 1984 dollars). The costs of each treatment phase were adjusted for background costs, based on the duration of the treatment phase, and the assumptions regarding maintenance care and survival discussed above in sections II.1.H.3 and II.1.H.4. For example, the initial care, which covers a three-month period, has a background medical cost of $747 ($2,988 per year × 3/12 months). This background cost was subtracted from the total cost for initial care of $10,590, to obtain an incremental cost of $9,843.

Link to Sections II.1.H.3 and II.1.H.4

The costs have also been updated to 1996 using the Medical Care Component of the Consumer Price Index (1984:1996 = 2.14). The results are shown in Table II.1-4. The final value in the table, $82,581, is the undiscounted estimate of the lifetime incremental direct medical costs for a cancer case.

Depending on how this value is to be used, it may be possible to adjust the cost components to better reflect the cancer(s) of interest. For example, if it is known that there is a substantially higher mortality rate (50 percent was used here), then the terminal cost component could be adjusted accordingly. Any application should clearly state that this value was based on numerous assumptions and represents and average of many, but not all, cancers that occur in the U.S.

Table II.1-4 Incremental Undiscounted Direct Medical Costs for a Typical Cancer

Treatment Phase	Total Medical Costs (1984$)	Incremental Medical Costs[a]	Incremental Medical Costs in 1996 Dollars[b]	Lifetime Incremental Costs[c]
Initial (3 months)	$10,590.00	$9,843.00	$21,064.02	$21,064.02
Maintenance	$600.46 (per month)	$351.46 (per month)	$752.12 (per month)	$45,127.46 (5 years)
Terminal (6 months)	$16,811.46	$15,317.46	$32,779.36	$16,389.68
Total Lifetime Costs in 1996 Dollars[d]				$82,581.16

a Adjusted for background medical costs of $2,988 per year (1984$), or $249 per month.
b Adjusted from 1984 to 1996 dollars using the medical care component of the Consumer Price Index (1984:1996=2.14).
c Five years of maintenance care were assumed and a mortality rate of 50 percent was assumed (i.e., the terminal care costs were multiplied by .5). See text for discussion.
d These costs can be updated to the current year using inflation factors accessible by clicking below.

Link to inflation factors

II.1.H.6. Application to Specific Cancers

II.I.H.6.1 Method

A more precise approach can be taken for specific cancers, if necessary, when sufficient statistics are available. The typical costs per treatment phase discussed above are used, with the maintenance phase and terminal care evaluated in more detail. The following components were used:

1) initial care — all patients receive initial care, so there are no modifications made to this phase's costs.

2) maintenance care — the length of the maintenance phase was estimated based on the survival probability of people of the average age of diagnosis. This duration of care was used to estimate costs for this phase.

Two specific cancers were evaluated, bone and liver cancer, in response to specific requirements of the Agency for an upcoming rule requiring benefits evaluations. The rule required only the direct medical costs for *survivors* of bone and liver cancer because the value of a statistical life (VSL) was to be used for nonsurvivors. The percentage of survivors and nonsurvivors for these cancer are discussed in Section II.I.H.6.4 below. Cost estimations were made using steps above. Two different approaches to estimating maintenance costs were used to illustrate alternative methods.

As noted above, the initial care costs shown in Table II.1-4 were used without modification for the costs of this phase. To determine the estimated cost for the maintenance period care for survivors, the length of the maintenance period was evaluated using two statistics:

1) the average ages at diagnosis for the two cancers were determined using the National Cancer Institute's SEER database, as described in Section II.1.G.2 above. The percent of all patients diagnosed in each age group was used to calculate the mean age at diagnosis (this is illustrated graphically in the stomach cancer chapter).

Link to Chapter II.2
Link to Chapter II.1.G.2

The average age at diagnosis for bone and liver cancer were determined to be 69 and 66 years, respectively.

2) The life expectancy of an average individual in the general population was determined for the two ages of diagnosis listed above from vital statistics data (accessed in 1998 from National Center for Health Statistics web site). They were determined to be 14.8 years (rounded to 15 years) for a 69-year-old bone cancer patient, and 16.7 years (rounded to 17 years) for a 66-year-old liver cancer patient. It was assumed that the life expectancy of survivors is the same as that of the general population. In reality, the treatments for cancer, including radiation, antineoplastic drugs, etc., have toxic effects that may shorten the lives of cancer patients. There are not sufficient data on these effects to quantitatively determine the impact.

II.I.H.6.2 Approach I.

The full term of care was assumed to be ten years. This duration is reasonable because nonsurvivors were not included, and the life expectancy at the average ages of diagnosis (66 and 69 years) is considerable (15 to 17 years). Additional care associated with cancer may not be required over the full remaining life of the individual. The first-year costs consisted of initial care costs ($21,064) and nine months of maintenance care ($753,12 × 9 = $6,769). (See Table II.1-4 for incremental costs for each phase of care.) The remaining nine years of maintenance care were added to initial costs to obtain the total estimated lifetime direct medical costs.

II.I.H.6.3 Approach II.

The maintenance phase was assumed to be equal to the life expectancy of the general population at the average age of diagnosis, minus three months of initial care. As in Approach I, the first year costs consisted of initial care costs and nine months of maintenance care. The remaining years of life (i.e., life expectancy at the average age at diagnosis minus the first year of

services) were multiplied by the annual maintenance care cost and added to initial costs to obtain the total estimated lifetime direct medical cost (i.e., 14 years for bone cancer and 16 years for liver cancer). This approach is reasonable because patients may require maintenance care over their remaining lifetime due to the drastic nature of most cancers, and the likely concurrent effects induced by surgery, radiation, and chemotherapy.

In the absence of accurate long-term treatment information for survivors, either approach may be used. They are both offered to provide a range of options for economists and to illustrate the impact of altering assumptions regarding care on medical cost estimates.

The results obtained using both approaches are shown in Table II.1-5 using discount rates of 0, 3, 5, and 7 percent. Bone cancer lifetime medical cost estimates for survivors range from $109,052 to $154,189 (undiscounted). Liver cancer lifetime medical cost for survivors range from $109,052 to $172,240 (undiscounted).

As the results indicate, maintenance care costs are a major portion of total medical costs for survivors. Differing assumptions regarding the duration of time over which these costs will occur lead to differences in overall lifetime cost estimates that are not trivial ($87,000 versus $151,000, undiscounted). These differences are relatively small, however, when contrasted with costs associated with the value of a statistical life (approximately $5,000,000). Although it is important to obtain medical cost estimates that are as precise as possible, in the case of fatal cancers (where the VSL is used for some patients) the differences between Approach I and Approach II do not substantially alter the final results of a benefits assessment.

As noted above, these costs are for survivors of the diseases only. It is relatively simple to calculate the costs for nonsurvivors if data are located on the timing of death. Terminal care costs are listed in Table II.1-4 and can be used, with the appropriate maintenance care costs, to estimate direct medical costs for nonsurvivors. Note that the maintenance costs estimated for survivors should not be used because they are likely to have a much longer duration of care than do nonsurvivors.

Table II.1-5 Estimated Incremental Direct Medical Costs for Bone and Liver Cancer Survivors[a] (1996 dollars)[b]

Type of Cancer and Approach[a]	Age at Diagnosis	Life Expect-ancy	Initial Care Costs	Maintenance Care Costs				Total Lifetime Costs			
				Discount Rates: 0	3	5	7	Discount Rates: 0	3	5	7
Bone	69	15	$21,064								
Approach I				87,988	77,042	70,920	65,572	$109,052	98,106	91,988	86,636
Approach II				133,125	108,721	96,108	85,700	$154,189	129,785	117,172	106,764
Liver	66	17	21,064								
Approach I				87,988	77,042	70,920	65,572	$109,052	98,106	91,988	86,636
Approach II				151,176	120,138	104,584	92,029	$172,240	141,202	125,648	113,093

a. See text for discussion of approaches.
b. These costs can be updated to the current year using inflation factors accessible by clicking below.

Link to inflation factors

II.1.H.6.4 Liver and Bone Cancer Survival Estimates

Because the VSL is sometimes used for nonsurvivors of bone and liver cancer, it is important to estimate the survival and mortality rates for these cancer patients. This was done using the RSR data from NCI as discussed in Section II.1.G.2 and presented in detail in Chapter II.2. Because the cost estimates for these two cancers are not precise (the costs for a "typical" cancer case were used, as described above), it was determined that the RSRs provided a reasonable approximation of the survival rate.

Link to Section II.1.G.2 and Chapter II.2

Ideally, one would determine the lifetime mortality impacts of these cancers on patients, which would require a lifetime follow-up. These data are not available. NCI provides a twenty-one year database (1973-1993) of the survival experience of liver cancer patients. That database was used in this analysis and provides a lower-bound estimate of mortality impacts. (It may slightly underestimate mortality because increased deaths may occur beyond the twenty-first year post-diagnosis. This increase, however, is not likely to be substantial.)

Bone cancer, which is rarer and less well studied, is included in the NCI grouping "bone and joint cancers." Consequently, the survival estimates are less precise for bone cancer. In addition, the RSR was available only for five years post-diagnosis for this group of cancers. The actual mortality rate is very likely to be greater than that observed at five years because mortality is typically elevated for more than five years post-diagnosis. Mortality will therefore be underestimated. Unfortunately, the dynamics of survival and relapse differ considerably among cancers, so it is not possible to estimate the longer-term survival for bone cancer based on mortality patterns for other cancers.

The NCI RSR data indicate that the survival rate for liver cancer is approximately 2.6 percent, indicating a 97.4 percent mortality rate (after 21 years). The bone and joint cancer survival rate is estimated to be 64.3 percent, indicating a 35.7 percent mortality rate (after five years).

II.1.H.7 Conclusions Regarding Typical Cancer Cost Estimates

There is clearly uncertainty when a "typical" cancer approach is used. As Table II.1-3 shows, however, there are relatively small differences among the medical costs of various cancers when contrasted with the uncertainty in risk estimations, changes in medical care and survival, and uncertainty associated with other parameters in a benefits assessment. The value in Table II.1-4 and approaches described above provide a means to obtain an estimate of cancer medical costs that may be useful in a benefits evaluation when limited data are available to support a full and detailed analysis of medical costs.

II.1.I Issues and Uncertainty in Cancer Medical Cost Estimation

Chapter I.1 contains a detailed discussion of numerous sources of uncertainty in medical cost estimation. Most issues related to estimating medical costs of specific types of cancer are discussed in the individual chapters, which also contain a detailed presentation of the methodologies used to estimate costs. Some issues are common to all cancers and are briefly discussed in this section. This section also contains the estimated lifetime medical costs for a "typical" cancer case. In addition, there are some uncertainties and issues that are particularly problematic for cancer cost estimation. These issues, discussed below, include new treatments that are developed (with attendant changes in cost) and concurrent effects associated with either the occurrence of the cancer or medical treatments for cancer.

Link to I.1.F: Limitations

II.1.I.1 New Treatments

The costs of new treatments are of particular concern in cancer therapy, because they may be very expensive, and because what is considered experimental at one time may soon become the treatment norm. For example, advances have been made very rapidly during the 1990s in the treatment of advanced stages of breast cancer. In the past, the prognosis was poor for advanced stages and the treatments limited. Consequently, economic valuations might include a value of life estimate rather than a medical cost estimate as the predominating cost factor. In recent years, however, more expensive and effective treatments, such as bone marrow transplants and new pharmaceuticals, have shifted the balance for this disease somewhat toward improved survival with a corresponding increase in medical costs. As a result of this dynamic, it is appropriate for an economic evaluation to include a review of recent literature to determine whether new treatment approaches with substantially different costs are being employed for a specific disease.

II.1.I.2 Concurrent Effects

As noted in Section II.1.B. above, concurrent effects are of particular concern for certain types of illnesses, including cancer and developmental effects (discussed in the next section). Cancer has a unique ability to metasticize, leading to multiple types of cancer in an individual. Cancer may also interfere with the functioning of various organs in the body, requiring medical attention above and beyond the cancer-limiting treatments. Finally, the treatments themselves, which often include ionizing radiation and highly toxic chemotherapeutics, may cause serious illnesses, including cancers at other sites in the body, impairment of the immune system, disabilities, and damage to the nervous system or other organs.

When data are not available on concurrent effects, and the chapter indicates that they are likely to occur (as is the case for all cancers), the medical cost estimates provided will underestimate total medical costs. This discrepancy should be noted when the costs are used.

All of these concurrent effects may occur during or significantly after the cancer occurrence. It is beyond the scope of this handbook to include a discussion of the multiple associated diseases that can arise from a specific cancer. This information may be important, however, to a comprehensive economic analysis. Where data are available regarding concurrent effects, they are described briefly in the cancer chapters. In addition, readers are urged to consult with the medical and toxicological sources providing the basic health risk information, in order to obtain additional data on likely concurrent effects arising from the diseases or their treatment.

Some cancer cost evaluations, such as those based on Baker et al. (i.e., lung, breast, liver, kidney, bladder, colorectal, and the "typical" cancer costs estimated in this chapter in the previous section) include all estimates of the incremental medical costs associated with a cancer diagnosis. These values are calculated by summing all medical costs and subtracting the background costs to obtain incremental costs. Using this approach, costs are included that may be cancer-related, but not specifically designed to address cancer. For example, immune-suppressed patients who are receiving radiation therapy may have greater costs associated with infectious diseases. The additional required services are due to cancer, but are not specifically designed to mitigate the cancer. Including these costs provides a more comprehensive and realistic estimate of the total medical cost of the disease.